

## CLAIMS:

1. A composition comprising a conjugate formed by
  - (a) a modified metallothionein (MT) amino acid sequence or fragment  
 5 thereof that binds the megalin receptor less avidly than naturally-occurring metallothionein; and
  - (b) at least one or multiple molecules of a therapeutic divalent metal ion.
2. The composition according to claim 1, wherein said modified MT does not  
 10 bind megalin.
3. The composition according to claim 1, wherein said modified MT comprises a modified  $\beta$  - MT subunit sequence  
 MDPNC<sub>1</sub> SC<sub>2</sub>ATGNSC<sub>3</sub>TC<sub>4</sub>ASSC<sub>5</sub>KC<sub>6</sub>KEC<sub>7</sub>KC<sub>8</sub>TSC<sub>9</sub>X SEQ ID NO: 2, wherein X  
 15 is any uncharged or negatively charged amino acid and is not K.
4. The composition according to claim 1, wherein said modified MT comprises a modified  $\alpha$  - MT subunit sequence  
 X'SC<sub>10</sub>C<sub>11</sub>SC<sub>12</sub>C<sub>13</sub>PAGC<sub>14</sub>TKC<sub>15</sub>AQGC<sub>16</sub>IC<sub>17</sub>KGASDKC<sub>18</sub>SC<sub>19</sub>C<sub>20</sub>A, SEQ ID NO:  
 20 3, wherein X' is any uncharged or negatively charged amino acid and is not K.
5. The composition according to claim 1, wherein said modified MT comprises a modified MT sequence  
 MDPNC<sub>1</sub> SC<sub>2</sub>ATGNSC<sub>3</sub>TC<sub>4</sub>ASSC<sub>5</sub>KC<sub>6</sub>KEC<sub>7</sub>KC<sub>8</sub>TSC<sub>9</sub>X X'SC<sub>10</sub>C<sub>11</sub>SC<sub>12</sub>C<sub>13</sub>PAGC<sub>14</sub>  
 25 TKC<sub>15</sub>AQGC<sub>16</sub>IC<sub>17</sub>KGASDKC<sub>18</sub>SC<sub>19</sub>C<sub>20</sub>A, SEQ ID NO: 4, wherein X and X' are independently selected from any uncharged or negatively charged amino acid and is not K.
6. The composition according to any of claims 3 to 5, wherein all C residues in  
 30 said sequence are invariant.

7. The composition according to claim 3 and 5, wherein said modified MT is truncated at the amino or carboxy terminus.
8. The composition according to any of claims 3 to 5, wherein X or X' is Q.
- 5 9. The composition according to any of claims 3 to 5, wherein any amino acid other than C is modified by substitution with a non-naturally-occurring amino acid.
- 10 10. The composition according to any of claims 3-5, wherein said modified MT comprises a fusion protein comprising multiple copies of full-length MT or subunit fragments thereof, wherein the fusion protein has an overall negative or neutral charge or a negative or neutral charge at the positions indicated by X and X'.
- 15 11. The composition according to claim 1, wherein said conjugate has a size greater than 70 kD.
- 20 12. The composition according to claim 1, wherein the number of molecules of heavy metals complexes to a single modified MT or fragment thereof range from 1 to 7.
13. The composition according to claim 1, wherein said divalent metal ions are selected from the group consisting of anti-neoplastic platinum compounds, cadmium, and copper.
- 25 14. The composition according to claim 1, wherein said conjugate further comprises
- (c) a delivery peptide for targeted delivery to a desired cell, wherein said delivery peptide is fused to said modified MT or fragment thereof.
- 30 15. The composition according to claim 1, further comprising a pharmaceutically acceptable carrier.

16. The composition according to claim 1, further comprising a second therapeutic compound or composition.
- 5 17. A method for treating cancer comprising administering to a mammalian subject an effective amount of the composition of claim 1, wherein said treatment inhibits the renal uptake of said divalent metal ions.
- 10 18. Use of the composition of claim 1 in the preparation of a medicament for the treatment of cancer.
19. A method for inhibiting renal uptake of therapeutic divalent metals ions comprising administering said ions as part of a conjugate of a composition of claim 1.
- 15 20. A metallothionein derivative amino acid sequence that does not bind megalin as avidly as naturally occurring metallothionein.